IN THE CLAIMS

Amend the claims as indicated below by the markings.

1. (Currently amended) ~~A non-human mutant mammal,~~ A mutant mouse deficient in an endogenous Sigma-1 receptor, whose genome comprises a mutation comprising a disruption in a gene of an endogenous Sigma-1 receptor, wherein said gene disruption gives rise to a ~~non-human mutant mammal~~ mutant mouse lacking detectable levels of endogenous Sigma-1 receptor.

2. (Currently amended) The ~~non-human mutant mammal~~ mutant mouse according to claim 1, wherein said ~~non-human mutant mammal~~ mutant mouse is a heterozygous mutant for said mutation.

3. (Currently amended) The ~~non-human mutant mammal~~ mutant mouse according to claim 1, wherein said ~~non-human mutant mammal~~ mutant mouse is a homozygous mutant for said mutation.

4. (Cancelled)

5. (Currently amended) The ~~non-human mutant mammal~~ mutant mouse according to claim 1, wherein the genome of the ~~non-human mutant mammal~~ mutant mouse comprises a transgene within the mutation introduced in the endogenous Sigma-1 receptor gene that comprises a gene encoding a positive selection marker.

6. (Currently amended) The ~~non-human mutant mammal~~ mutant mouse according to claim 5, wherein said transgene comprises the neomycin phototransferase (*neo*) gene.

7. (Cancelled)

8. (Currently amended) The ~~non-human mutant mammal~~ mutant mouse according to claim 1, wherein said ~~non-human mutant mammal~~ mutant mouse is ~~a mutant mouse,~~ deficient in the endogenous

Sigma-1 receptor, homozygous for the mouse Sigma-1 receptor gene, and fertile, whose genome contains a disruption in said gene comprising the *neo* gene.

9. (Currently amended) A homologous recombination vector with positive-negative selection, comprising:

a first homology region positioned at the 5' end of a nucleotide sequence encoding a positive selection marker, wherein said first homology region has a nucleotide sequence that is substantially identical to a first sequence of a Sigma-1 receptor gene;

a nucleotide sequence encoding a positive selection marker;

a second homology region positioned at the 3' end of said nucleotide sequence encoding a positive selection marker, wherein said second homology region has a nucleotide sequence that is substantially identical to a second nucleotide sequence of said Sigma-1 receptor gene, this second sequence of the Sigma-1 receptor gene being positioned at 3' to the first sequence of the Sigma-1 receptor gene in a wild type endogenous Sigma-1 gene; and

a nucleotide sequence encoding a negative selection marker.

10. (Cancelled)

11. (Previously amended) A vector according to claim 9, wherein said second nucleotide sequence encoding a positive selection marker comprises a neomycin phototransferase (*neo*) gene.

12. (Previously amended) The vector according to claim 9, wherein said nucleotide sequence encoding a positive selection marker comprises a thymidin kinase (*tk*) gene of the herpes simplex virus (HSV).

13. (Previously amended) The vector according to claim 9, identified as pHR53TK, deposited in Spanish Type Culture Collection (CECT) of the University of Valencia with access number CECT 5737.

14. (Currently amended) A host cell whose genome comprises an endogenous Sigma-1 receptor gene transfected with a homologous recombination vector with positive-negative selection according to claim 9, deficient in an endogenous Sigma-1 receptor.

15. (Currently amended) The cell according to claim 14, wherein said host cell whose genome contains an endogenous Sigma-1 receptor gene is selected from the group consisting of a differentiated cell that normally expresses the product of the Sigma-1 receptor gene and a pluripotent embryonic cell.

16. (Previously amended) The cell according to claim 14, comprising an allele of the mutated Sigma-1 receptor gene.

17. (Currently amended) An isolated cell from a non-human mutant mammal, deficient in an endogenous Sigma-1 receptor, according to claim 1, or its offspring.

18. (Currently amended) The cell according to claim 17, comprising one or both mutated alleles of the Sigma-1 receptor gene.

19. (Previously amended) The cell according to claim 17, wherein the cell is propagated.

20. (Currently amended) The offspring of a ~~non-human mutant mammal~~ mutant mouse deficient in an endogenous Sigma-1 receptor, according to claim 1.

21. (Currently amended) A process for making a ~~non-human mutant mammal~~ mutant mouse according to claim 1, comprising:

introducing a functional disruption in an endogenous Sigma-1 receptor gene present in a cell genome by homologous recombination in said cell between an allele of an endogenous Sigma-1 receptor gene and a homologous recombination vector with positive-negative selection according to claim 9,

selecting the recombinant homologues by the positive-negative selection technique,

introducing said recombinant homologues in embryos,

implanting said embryos receptor pseudogestating female mammals,

carrying, by the female mammals, the embryos to term,

selecting chimeras able to efficiently transmit the genotype of the recombinant homologues to their offspring by the germ line, and

crossing said chimeras with ~~non-human~~ wild-type mice ~~mammals~~ to obtain heterozygous mutants to disrupt the endogenous Sigma-1 receptor.

22. (Currently amended) A method for utilizing a ~~non-human mutant mammal~~ mutant mouse according to claim 1, comprising:

providing the mouse ~~the mammal~~ as a control animal; and

conducting *in vivo* tests utilizing the ~~mammal~~ mouse.

23. (Currently amended) A method for utilizing a ~~non-human mutant mammal~~ mutant mouse deficient in the Sigma-1 receptor, or of a cell line deficient in the Sigma-1 receptor, comprising:

evaluating potentially useful compounds designed to perform at least one of the following functions:

at least one of preventing or treating disorders of the central nervous system;

at least one of preventing or treating memory alterations;

at least one of preventing or treating stress conditions;

at least one of preventing or treating drug addiction conditions;

producing analgesia; and

producing neuroprotection.

24. (Cancelled)

25. (Currently amended) A method for determining an effect of a compound to be tested on a ~~non-human mammal~~ mutant mouse deficient in an endogenous Sigma-1 receptor, comprising:

placing in contact a ~~non-human mutant mammal~~ mutant mouse according to claim 1 with said compound, and

detecting a presence or absence of a physiological change in said ~~non-human mutant mammal~~ mutant mouse in response to the contact with said compound.

26. (Currently amended) A method for determining an effect of a compound to be tested on a ~~non-human mammal~~ mutant mouse deficient in an endogenous Sigma-1 receptor, comprising:

administering said compound to be tested to a ~~non-human mutant mammal~~ mutant mouse according to claim 1;

administering said compound to be tested to a control mouse ~~non-human mammal~~ expressing a functional endogenous Sigma-1 receptor; and

observing if said compound has an effect on a phenotype of said ~~non-human mutant mammal~~ mutant mouse when compared to the control mouse ~~non-human mammal~~.

27. (Currently amended) A method for determining an effect of a compound on cells expressing a Sigma-1 receptor and on cells not expressing said Sigma-1 receptor, comprising:

introducing a compound to be tested in a cell population or in a homogenisation thereof, wherein said cells are isolated established cells from a ~~non-human mutant mammal~~ mutant mouse according to claim 1,

administering said compound to be tested to a population of control mouse ~~non-human mammal~~ cells or to a homogenisation thereof, which expresses a functional Sigma-1 receptor, and

observing or analysing whether said compound to be tested has an effect on the expression of said Sigma-1 receptor in the cells of said ~~non-human mutant mammal~~ mutant mouse when compared to the cells of a control ~~non-human mammal~~ mouse.

28. (Previously presented) The cell according to claim 19 wherein the cell is immortalized.

29. (Previously presented) The process according to claim 21, further comprising:

crossing said heterozygous mutants with each other to obtain homozygous mutants.

30. (New) The mutant mouse according to claim 1, wherein said mouse is fertile and obtainable by the use of the vector identified as pHR53TK that is deposited in the CECT under access number CECT 5737, to insert a functional disruption in the endogenous Sigma-1 receptor.